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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/970,607	10/03/2001	Valerie L. Gerlach	15966-675 CIP 2 (Cura-175)	2700
30623	7590	12/06/2004	EXAMINER	
MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C. ONE FINANCIAL CENTER BOSTON, MA 02111			MERTZ, PREMA MARIA	
			ART UNIT	PAPER NUMBER
			1646	

DATE MAILED: 12/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/970,607	GERLACH ET AL.	
	Examiner	Art Unit	
	Prema M Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5,9,10,12-14 and 80 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5,9,10,12-14 and 80 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>12/12/01</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Restriction/Election

1. Applicant's election of Group II (claims 5-14, 30, 33, 36, 48-57, 69 and 72) on 2/3/04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-4, 6-8, 11, 15-79 have been canceled on 2/3/04. Amended claims 5, 9, 10, 12 (2/3/04), original claims 13, 14 and new claim 80 (2/3/04) are pending and under consideration by the Examiner.

Priority

2. According to the priority statement of 10/3/2001, it appears that priority is being claimed to a large number of provisional applications. These applications appear to be drawn to unrelated subject matter and are either not available for consideration or for which consideration to determine support for the instantly claimed subject matter would require an undue burden. Accordingly, the subject matter defined in claims 5, 9, 10, 12-14, 80 has an effective filing date of 10/3/2001, that of the instant application. Applicants are requested to provide the serial number and specific page numbers of any parent application to which priority is desired which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession and fully enabled prior to 10/3/2001.

Specification

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3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

Claim Rejections - 35 USC § 101 and § 112

4. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 5, 9-10, 12-14, 80 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation.

The instant claims are drawn to a nucleic acid encoding a polypeptide which has an as yet undetermined function or biological significance but is referred to as NOV2 (pages 9-11). Until some actual and specific significance can be attributed to the protein identified in the specification as having homology to (page 9, lines 24-30), the instant invention is incomplete. The translation product of the claimed protein encoded by the nucleic acid of SEQ ID NO:3, shares sequence homology (95% identity) with an uncharacterized region of human chromosome

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X, including clone r11-382F24 (CHR X; EMBL Accession No.: 158819), as is shown in Table 6. Also, a NOV2 polypeptide has homology (81% identity, 86% similarity) with a member of the GAGE gene family, human PAGE-Z polypeptide (PAGEZ; PatP Accession No.: Y83168), as is shown in Table 7. Further, a NOV2 polypeptide has homology with another member of the GAGE gene family, PAGE-I (PAGEI; GenBank Accession No.: AAC25990.1), as is shown in Table 8. However, the instant specification does not disclose any information regarding functional characteristics or the biological activity of the instantly claimed nucleic acid encoding the protein of amino acid sequence set forth in SEQ ID NO:4. While the specification on page 11 describes many diseases for which the NOV2 protein can be used, the disease conditions ranging from prostate cancer, melanoma and diseases of reproductive health, there is no disclosure of the role the NOV2 protein may play in any of these conditions, and there is no guidance given about which specific activity/activities the polypeptide would be likely to have. The specification does not demonstrate that the polypeptide actually displays any activity to treat any of these disparate diseases. In the absence of knowledge of the specific biological significance of the protein, there is no immediately obvious patentable use for it. Since the instant specification does not disclose a "real world" use for the nucleic acid encoding the protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 USC § 101 as being useful.

A protein of unknown function would have utility if it can be employed as an indicator of a diseased state or of the presence of a disorder. However, Applicants have failed to show any differential expression of the instant protein in normal tissue and in any disease tissue. Applicant is only required to identify one substantial credible utility and the employment of this protein

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only as the subject of further research does not satisfy the utility requirement of 35 U.S.C. § 101 because the courts have interpreted this statute as requiring an invention to have "substantial utility" "where specific benefit exists in currently available form". The employment of a protein of the instant invention, in the treatment of the various recited diseases on page 11 is not a substantial or specific utility.

Applicants disclose in the specification that the claimed protein has homology to (95% identity) an uncharacterized region of human chromosome X, including clone r11-382F24 (CHR X; EMBL Accession No.: 158819), as is shown in Table 6. Also, a NOV2 polypeptide has homology (81% identity, 86% similarity) with a member of the GAGE gene family, human PAGE-Z polypeptide (PAGEZ; PatP Accession No.: Y83168), as is shown in Table 7. Further, a NOV2 polypeptide has homology with another member of the GAGE gene family, PAGE-I (PAGEI; GenBank Accession No.: AAC25990.1), as is shown in Table 8. The state of the art is such that functional information can be automatically derived from structural information only to a limited extent, (see Sklonick et al, Nature Biotechnology, Vol.18, No.3, pages 283-287, especially page 286, middle of column 1). Sklonick et al also state that knowledge of the overall structure or domain family is still not enough to confidently assign function to a protein. Therefore, there is little doubt that, after further characterization, the protein is found to be member of the GAGE gene family, the claimed protein would have a specific, substantial and credible utility. However, further characterization is part of the invention and until it had been undertaken, the claimed invention is not supported by a specific asserted utility or a well established utility. The claimed invention is directed to a polypeptide of as yet undetermined function or biological significance. Thus, since there is no biological activity disclosed for the

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protein encoded by the claimed nucleic acid, the claimed invention is not supported by either a specific and substantially asserted utility or a well established utility.

There is little doubt that, after complete characterization, the claimed nucleic acid encoding the protein of SEQ ID NO:4 will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicants claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the Court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The Court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Because the claimed invention is not supported by a specific asserted utility for the reasons set forth above, credibility cannot be ascertained.

On page 11, Applicants disclose that NOV2 can be used to detect prostate, placental and newborn tissue (page 11, lines 4-6). The employment of a protein of the instant invention, or a nucleic acid encoding that protein, as a tissue specific marker is not a substantial or specific

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utility. All human proteins can invariably be classified into two categories, those which are expressed in a tissue or developmentally specific manner and those which are expressed ubiquitously. It can be alleged that any protein which is expressed in a tissue specific manner can be employed to detect the tissue in which it is expressed in a sample. Alternately, a human protein which is expressed ubiquitously can be employed to detect the presence of any human tissue in a sample. Such utilities are analogous to the assertion that a particular protein can be employed as a molecular weight marker, which is neither a specific or substantial utility.

Claims 5, 9-10, 12-14, 80, are also rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

4. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a host cell in culture comprising a polynucleotide with the sequence as set forth in SEQ ID NO: 3, does not reasonably provide enablement for *in vivo* transfection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification discloses that the nucleic acids of the current invention can be expressed in a wide variety of host cell types, including cells within a host animal (page 86-87). However, there are no actual or prophetic examples that disclose how to make or use host cells that comprise a DNA sequence as set forth in SEQ ID NO: 3 in an animal. The Examiner cites Eck & Wilson (page 81, column 2, second paragraph to page 82, column 1, second paragraph)

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who report that numerous factors complicate *in vivo* gene expression which have not been shown to be overcome by routine experimentation. These include, the fate of the DNA vector itself (volume distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. Since the instant disclosure does not address any of the methods necessary to make a host cell in an animal, which comprises the polynucleotide of interest, the claims as written are not enabled. This rejection could be overcome by addition of the limitation wherein the host cells are "isolated".

6. Claim 80 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule encoding a polypeptide comprising an amino acid sequence set forth in SEQ ID NO:4, does not reasonably provide enablement for a nucleic acid molecule comprising a complement of a nucleotide sequence encoding a polypeptide comprising an amino acid sequence set forth in SEQ ID NO:4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

With respect to claim 10, as recited, the claim encompasses a complement of a nucleic acid molecule encoding a polypeptide set forth in SEQ ID NO:4. The specification is non-enabling for a complement of a nucleic acid molecule encoding a polypeptide set forth in SEQ ID NO:4 because the specification does not provide the guidance to make a complement of a

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nucleic acid molecule that could encode a polypeptide having the amino acid sequence as set forth in SEQ ID NO:4. The instant specification is non-enabling for such, because how can one make a nucleic acid and a complement thereof, both encoding the same amino acid sequence. The specification provides no guidance and in the absence of such a disclosure, a skilled artisan would be unable to make/use the complement of a nucleic acid encoding a polypeptide set forth in SEQ ID NO:4, as embraced by the claim. It is suggested that the claim be amended to recite "a nucleic acid molecule encoding a polypeptide set forth in SEQ ID NO:4 or the complement thereof".

Claim rejections-35 USC § 112, second paragraph

7. Claims 10, 12-13, 80 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is vague and indefinite for several reasons.

Claim 10 recites "hybridizes under stringent conditions", which is a relative and conditional term and renders the claim indefinite. Furthermore, some nucleic acids which might hybridize under conditions of moderate stringency, for example, would fail to hybridize at all under conditions of high stringency. The metes and bounds of the claim thus cannot be ascertained. This rejection could be obviated by supplying specific conditions supported by the specification which Applicants consider to be "stringent".

Furthermore, claim 10 is vague and indefinite in the recitation of "said nucleic acid molecule hybridizes under stringent conditions to SEQ ID NO:3". It is inconceivable that the same/identical coding nucleic acid strands can hybridize to each other. It is suggested that the

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claim be amended to recite "said nucleic acid molecule hybridizes under stringent conditions to the complement of SEQ ID NO:3".

Claims 12-13 are vague and indefinite because of the recitation of "a vector...". It is suggested that the claims be amended to recite "a recombinant expression vector" for which there is a basis in the instant specification (see page 85, lines 20-21.

Claim 80 is vague and indefinite in the recitation of " a complement of a nucleic acid molecule encoding a polypeptide set forth in SEQ ID NO:4". It is inconceivable that both the nucleic acid and its complementary strand can encode a polypeptide as set forth in SEQ ID NO:4. It is suggested that the claim be amended to recite "a nucleic acid molecule encoding a polypeptide set forth in SEQ ID NO:4 or the complement thereof".

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims are rejected under 35 U.S.C. 102(a) and 35 U.S.C. 102(e) as being anticipated by WO 01/61009.

The reference discloses a NOV2 nucleotide sequence of SEQ ID NO:3 encoding a polypeptide of amino acid sequence shown SEQ ID NO:4 (pages 8-10). A copy of the comparison of SEQ ID NO:1 of the polypeptide of the instant invention and the polypeptide

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disclosed in the reference is enclosed at the end of this action (SEQUENCE COMPARISON A). The reference also discloses that the nucleic acid encoding the protein was cloned into an expression vector, which contains a promoter operably linked to the nucleic acid insert encoding the protein (pages 86-90). Host cells were transformed with the DNA in the vector (pages 89-90). Therefore, the nucleic acid disclosed in the reference meets the limitations of claims 5, 9, 10, 12-14 and 80.

Applicants are advised that once priority is perfected to a provisional application which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession and fully enabled prior to 10/3/2001, this rejection will be withdrawn.

Conclusion

No claim is allowable.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz
Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
September 1, 2004

GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: June 15, 2004, 10:01:55 ; Search time 55 Seconds
(without alignments)
570.232 Million cell updates/sec

Title: US-09-970-607-4

Perfect score: 571

Sequence: 1 MSEHVRTRSSQSRGNDQES.....EGIMPTDLTKVLEAGDAQP 111

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 1586107 seqs, 282547505 residues

Total number of hits satisfying chosen parameters: 1586107

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database :

A_Geneseq_29Jan04:*

1: Geneseq1980s:*

2: Geneseq1990s:*

3: Geneseq2000s:*

4: Geneseq2001s:*

5: Geneseq2002s:*

6: Geneseq2003as:*

7: Geneseq2003bs:*

8: Geneseq2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB	ID	Description
1	571	100.0	111	4	Aae08581	Aae08581 Human NOV
2	571	100.0	111	6	Abj19255	Abj19255 Human can
3	537	94.0	111	4	Aae08582	Aae08582 Human NOV
4	537	94.0	111	4	Aae08593	Aae08593 Protein e
5	495.5	86.8	110	6	Abj19247	Abj19247 Human can
6	495.5	86.8	110	6	Abu56511	Abu56511 Lung can
7	495.5	86.8	110	6	Abj19247	Abj19247 Human can
8	450.5	78.9	94	4	Aae08580	Aae08580 Human NOV
9	438	76.7	109	3	Aay83168	Aay83168 PAGE2 pol
10	194	34.0	87	3	Aay83167	Aay83167 PAGE1 pol
11	181.5	31.8	102	3	Aay83158	Aay83158 PAGE-4 po
12	181.5	31.8	102	3	Aay52998	Aay52998 Human sec
13	181.5	31.8	102	5	Aae14575	Aae14575 Human dif
14	181.5	31.8	102	7	Abd75362	Abd75362 Prostate
15	171	29.9	111	4	Aam39588	Aam39588 Human pol
16	171	29.9	111	6	Abu57640	Abu57640 Different
17	171	29.9	111	6	Abj19256	Abj19256 Human can
18	171	29.9	111	6	Abc025121	Abc025121 Human GAG
19	171	29.9	111	7	Adc24650	Adc24650 Protein e
20	168	29.4	112	4	Abg05297	Abg05297 Novel hum
21	159	27.8	106	4	Aam41374	Aam41374 Human pol
22	153	26.8	111	4	Ab60500	Ab60500 Human cel
23	153	26.8	111	4	Aam78785	Aam78785 Human pro
24	153	26.8	111	5	Abb05753	Abb05753 Human G p
25	153	26.8	111	6	Abj19257	Abj19257 Human can

ALIGNMENTS

RESULT 1

AAE08581

ID AAE08581 standard; protein; 111 AA.

XX AC AAE08581;

XX

DT 01-NOV-2001 (first entry)

XX

DE Human NOV2 protein.

XX

KW Human; NOVX; G-antigen; GAGE-like protein; interferon;

KW G-protein coupled receptor; GPCR; hepatocyte nuclear factor;

KW mast cell protease; gene therapy; proliferative disorder; cancer;

KW immune disorder; hepatic disorder; cirrhosis; viral infection; hepatitis;

KW neurocognitive system-related disorder; neurological disorder;

KW Parkinson's disease; infertility; autoimmune disease; arthritis;

KW multiple sclerosis; allergy; wound healing; cytostatic; nootropic;

KW immunosuppressive; neuroprotective; vulnerary; hepatotropic.

XX OS Homo sapiens.

XX

XX WO200161009-A2.

XX

XX 23-AUG-2001.

XX 15-FEB-2001; 2001WO-US0004828.

XX 15-FEB-2000; 2000US-0182723P.

XX 15-FEB-2000; 2000US-0182724P.

XX 15-FEB-2000; 2000US-0182733P.

XX 22-FEB-2000; 2000US-0183896P.

XX 23-FEB-2000; 2000US-0184275P.

XX 23-FEB-2000; 2000US-0184482P.

XX 23-FEB-2000; 2000US-0184497P.

XX 24-FEB-2000; 2000US-0184744P.

XX 13-APR-2000; 2000US-0197083P.

XX 10-AUG-2000; 2000US-0224157P.

XX 18-SEP-2000; 2000US-0233405P.

XX 27-SEP-2000; 2000US-0236060P.

XX 02-JAN-2001; 2001US-0259414P.

XX 18-JAN-2001; 2001US-0262454P.

XX 14-FEB-2001; 2001US-00783429.

XX (CURA-) CURAGEN CORP.

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